

WHAT IS CLAIMED IS:

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1. A substantially pure  $\alpha$ -conotoxin peptide having the generic formula I: Xaa<sub>1</sub>-Xaa<sub>2</sub>-Xaa<sub>3</sub>-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Cys-Cys-Xaa<sub>6</sub>-Xaa<sub>7</sub>-Xaa<sub>8</sub>-Xaa<sub>9</sub>-Cys-Xaa<sub>10</sub>-Xaa<sub>11</sub>-Xaa<sub>12</sub>-Cys-Xaa<sub>13</sub> (SEQ ID NO1:), wherein Xaa<sub>1</sub> is des-Xaa<sub>1</sub>, Ile, Leu or Val; Xaa<sub>2</sub> is des-Xaa<sub>2</sub>, Ala or Gly; Xaa<sub>3</sub> is des-Xaa<sub>3</sub>, Gly, Trp (D or L), neo-Trp, halo-Trp or any unnatural aromatic amino acid; Xaa<sub>4</sub> is des-Xaa<sub>4</sub>, Asp, Phe, Gly, Ala, Glu,  $\gamma$ -carboxy-Glu (Gla) or any unnatural aromatic amino acid; Xaa<sub>5</sub> is Glu, Gla, Asp, Ala, Thr, Ser, Gly, Ile, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>6</sub> is Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>7</sub> is Asp, Glu, Gla, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>8</sub> is Ser, Thr, Asn, Ala, Gly, His, halo-His, Pro or hydroxy-Pro; Xaa<sub>9</sub> is Thr, Ser, Ala, Asp, Asn, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>10</sub> is Gly, Ser, Thr, Ala, Asn, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>11</sub> is Gln, Leu, His, halo-His, Trp (D or L), halo-Trp, neo-Trp, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid or any unnatural aromatic amino acid; Xaa<sub>12</sub> is Asn, His, halo-His, Ile, Leu, Val, Gln, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>13</sub> is des-Xaa<sub>13</sub>, Val, Ile, Leu, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; and the C-terminus contains a free carboxyl group or an amide group.
  2. A substantially pure  $\alpha$ -conotoxin peptide of generic formula I selected from the group consisting of:
    - Asp-Xaa<sub>1</sub>-Cys-Cys-Ser-Asp-Ser-Arg-Cys-Gly-Xaa<sub>2</sub>-Asn-Cys-Leu (SEQ ID NO:4);
    - Ala-Cys-Cys-Ser-Asp-Arg-Arg-Cys-Arg-Xaa<sub>3</sub>-Arg-Cys (SEQ ID NO:5);
    - Phe-Thr-Cys-Cys-Arg-Arg-Gly-Thr-Cys-Ser-Gln-His-Cys (SEQ ID NO:6);

Asp-Xaa<sub>4</sub>-Cys-Cys-Arg-Arg-His-Ala-Cys-Thr-Leu-Ile-Cys (SEQ ID NO:7);  
Asp-Xaa<sub>4</sub>-Cys-Cys-Arg-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Thr-Leu-Ile-Cys (SEQ ID NO:8);  
Gly-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Arg-Xaa<sub>4</sub>-Arg-Cys-Arg (SEQ ID NO:9);  
Gly-Gly-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Ala-Xaa<sub>3</sub>-Arg-Cys (SEQ ID NO:10);  
Ile-Ala-Xaa<sub>3</sub>-Asp-Ile-Cys-Cys-Ser-Xaa<sub>1</sub>-Xaa<sub>5</sub>-Asp-Cys-Asn-His-Xaa<sub>2</sub>-Cys-Val (SEQ  
ID NO:11); and

Gly-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Xaa<sub>2</sub>-His-Gln-Cys (SEQ ID NO:12),

wherein Xaa<sub>1</sub> is Glu or  $\gamma$ -carboxy-Glu (Gla); Xaa<sub>2</sub> is Lys, N-methyl-Lys, N,N-dimethyl-Lys  
or N,N,N-trimethyl-Lys; Xaa<sub>3</sub> is Trp (D or L), halo-Trp or neo-Trp; Xaa<sub>4</sub> is Tyr, nor-Tyr,  
mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa<sub>5</sub> is Pro or  
hydroxy-Pro; and the C-terminus contains a carboxyl or amide group, or derivatives thereof.

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3. The substantially pure  $\alpha$ -conotoxin peptide of claim 2, wherein Xaa<sub>1</sub> is Glu.
4. The substantially pure  $\alpha$ -conotoxin peptide of claim 2, wherein Xaa<sub>2</sub> is Lys.
5. The substantially pure  $\alpha$ -conotoxin peptide of claim 2, wherein Xaa<sub>4</sub> is Tyr.
- 15 6. The substantially pure  $\alpha$ -conotoxin peptide of claim 2, wherein Xaa<sub>4</sub> is mono-iodo-Tyr.
7. The substantially pure  $\alpha$ -conotoxin peptide of claim 2, wherein Xaa<sub>4</sub> is di-iodo-Tyr.
8. The substantially pure  $\alpha$ -conotoxin peptide of claim 1, which is modified to contain an O-glycan, an S-glycan or an N-glycan.
- 10 9. The substantially pure  $\alpha$ -conotoxin peptide of claim 2 which is modified to contain an O-glycan, an S-glycan or an N-glycan.
- 10 A substantially pure  $\alpha$ -conotoxin peptide having the generic formula II: Xaa<sub>1</sub>-Xaa<sub>2</sub>-Xaa<sub>3</sub>-Xaa<sub>4</sub>-Cys-Cys-Xaa<sub>5</sub>-Xaa<sub>6</sub>-Xaa<sub>7</sub>-Xaa<sub>8</sub>-Cys-Xaa<sub>9</sub>-Xaa<sub>10</sub>-Xaa<sub>11</sub>-Xaa<sub>12</sub>-Xaa<sub>13</sub>-Xaa<sub>14</sub>-Cys-Xaa<sub>15</sub>-Xaa<sub>16</sub>-Xaa<sub>17</sub> (SEQ ID NO:2), wherein Xaa<sub>1</sub> is des-Xaa<sub>1</sub>, Asp, Glu or  $\gamma$ -carboxy-Glu (Gla);

Xaa<sub>2</sub> is des-Xaa<sub>2</sub>, Gln, Ala, Asp, Glu, Gla; Xaa<sub>3</sub> is des-Xaa<sub>3</sub>, Gly, Ala, Asp, Glu, Gla, Pro or hydroxy-Pro; Xaa<sub>4</sub> is des-Xaa<sub>4</sub>, Gly, Glu, Gla, Gln, Asp, Asn, Pro or hydroxy-Pro; Xaa<sub>5</sub> is Ser, Thr, Gly, Glu, Gla, Asn, Trp (D or L), neo-Trp, halo-Trp, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>6</sub> is Asp, Asn, His, halo-His, Thr, Ser, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>7</sub> is Pro or hydroxy-Pro; Xaa<sub>8</sub> is Ala, Ser, Thr, Asp, Val, Ile, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>9</sub> is Gly, Ile, Leu, Val, Ala, Thr, Ser, Pro, hydroxy-Pro, Phe, Trp (D or L), neo-Trp, halo-Trp, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid or any unnatural aromatic amino acid; Xaa<sub>10</sub> is Ala, Asn, Phe, Pro, hydroxy-Pro, Glu, Gla, Gln, His, halo-His, Val, Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>11</sub> is Thr, Ser, His, halo-His, Leu, Ile, Val, Asn, Met, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>12</sub> is Asn, Pro, hydroxy-Pro, Gln, Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>13</sub> is des-Xaa<sub>13</sub>, Gly, Thr, Ser, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>14</sub> is des-Xaa<sub>14</sub>, Ile, Val, Asp, Leu, Phe, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; and Xaa<sub>15</sub> is des-Xaa<sub>15</sub>, Gly, Ala, Met, Ser, Thr, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>16</sub> is des-Xaa<sub>16</sub>, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-

Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>17</sub> is des-Xaa<sub>17</sub>, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; and the C-terminus contains a free carboxyl group or an amide group.

- 5 11. A substantially pure  $\alpha$ -conotoxin peptide of generic formula II selected from the group consisting of:

Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Ala-Cys-Xaa<sub>2</sub>-Gln-Thr-Xaa<sub>5</sub>-Gly-Cys-Arg (SEQ ID NO:13);  
 Cys-Cys-Xaa<sub>1</sub>-Asn-Xaa<sub>5</sub>-Ala-Cys-Arg-His-Thr-Gln-Gly-Cys (SEQ ID NO:14);  
 Gly-Cys-Cys-Xaa<sub>3</sub>-His-Xaa<sub>5</sub>-Ala-Cys-Gly-Arg-His-Xaa<sub>4</sub>-Cys (SEQ ID NO:15);  
 Ala-Xaa<sub>5</sub>-Cys-Cys-Asn-Asn-Xaa<sub>5</sub>-Ala-Cys-Val-Xaa<sub>2</sub>-His-Arg-Cys (SEQ ID NO:16);  
 Ala-Xaa<sub>5</sub>-Gly-Cys-Cys-Asn-Asn-Xaa<sub>5</sub>-Ala-Cys-Val-Xaa<sub>2</sub>-His-Arg-Cys (SEQ ID NO:17);  
 Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Cys-Asn-Asn-Xaa<sub>5</sub>-Ala-Cys-Val-Xaa<sub>2</sub>-His-Arg-Cys (SEQ ID NO:18);  
 Asp-Xaa<sub>1</sub>-Asn-Cys-Cys-Xaa<sub>3</sub>-Asn-Xaa<sub>5</sub>-Ser-Cys-Xaa<sub>5</sub>-Arg-Xaa<sub>5</sub>-Arg-Cys-Thr (SEQ ID NO:19);  
 Gly-Cys-Cys-Ser-Thr-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ala-Val-Leu-Xaa<sub>4</sub>-Cys (SEQ ID NO:20);  
 Gly-Cys-Cys-Gly-Asn-Xaa<sub>5</sub>-Asp-Cys-Thr-Ser-His-Ser-Cys (SEQ ID NO:21);  
 Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ala-His-Asn-Asn-Xaa<sub>5</sub>-Asp-Cys-Arg (SEQ ID NO:42);  
 Gly-Cys-Cys-Xaa<sub>4</sub>-Asn-Xaa<sub>5</sub>-Val-Cys-Xaa<sub>2</sub>-Xaa<sub>2</sub>-Xaa<sub>4</sub>-Xaa<sub>4</sub>-Cys-Xaa<sub>3</sub>-Xaa<sub>2</sub> (SEQ ID NO:154);  
 Xaa<sub>6</sub>-Xaa<sub>1</sub>-Xaa<sub>5</sub>-Gly-Cys-Cys-Arg-His-Xaa<sub>5</sub>-Ala-Cys-Gly-Xaa<sub>2</sub>-Asn-Arg-Cys (SEQ ID NO:155);  
 Cys-Cys-Ala-Asp-Xaa<sub>5</sub>-Asp-Cys-Arg-Phe-Arg-Xaa<sub>5</sub>-Gly-Cys (SEQ ID NO:156);  
 Gly-Cys-Cys-Xaa<sub>4</sub>-Asn-Xaa<sub>5</sub>-Ser-Cys-Xaa<sub>3</sub>-Xaa<sub>5</sub>-Xaa<sub>2</sub>-Thr-Xaa<sub>4</sub>-Cys-Ser-Xaa<sub>3</sub>-Xaa<sub>2</sub> (SEQ ID NO:157);  
 Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Thr-Cys-Xaa<sub>2</sub>-Xaa<sub>1</sub>-Thr-Xaa<sub>4</sub>-Gly-Cys (SEQ ID NO:158);  
 Cys-Cys-Ala-Asn-Xaa<sub>5</sub>-Ile-Cys-Xaa<sub>2</sub>-Asn-Thr-Xaa<sub>5</sub>-Gly-Cys (SEQ ID NO:159);  
 Cys-Cys-Asn-Asn-Xaa<sub>5</sub>-Thr-Cys-Xaa<sub>2</sub>-Xaa<sub>1</sub>-Thr-Xaa<sub>4</sub>-Gly-Cys (SEQ ID NO:160);  
 Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Val-Cys-Xaa<sub>2</sub>-Xaa<sub>1</sub>-Thr-Xaa<sub>4</sub>-Gly-Cys (SEQ ID NO:161);

Gly-Gly-Cys-Cys-Ser-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ile-Ala-Ser-Asn-Xaa<sub>5</sub>-Xaa<sub>2</sub>-Cys-Gly (SEQ ID NO:162);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Val-Cys-Ser-Ala-Met-Ser-Xaa<sub>5</sub>-Ile-Cys (SEQ ID NO:163);

Gly-Cys-Cys-Xaa<sub>2</sub>-Asn-Xaa<sub>5</sub>-Xaa<sub>4</sub>-Cys-Gly-Ala-Ser-Xaa<sub>2</sub>-Thr-Xaa<sub>4</sub>-Cys (SEQ ID NO:164);

Gly-Cys-Cys-Ser-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Phe-Ala-Thr-Asn-Xaa<sub>5</sub>-Asp-Cys (SEQ ID NO:165);

Gly-Gly-Cys-Cys-Ser-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ile-Ala-Asn-Asn-Xaa<sub>5</sub>-Leu-Cys-Ala (SEQ ID NO:166);

Gly-Gly-Cys-Cys-Ser-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ile-Ala-Asn-Asn-Xaa<sub>5</sub>-Phe-Cys-Ala (SEQ ID NO:167);

Asp-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ser-Gln-Asn-Asn-Xaa<sub>5</sub>-Asp-Cys-Met (SEQ ID NO:168); and

Asp-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ala-His-Asn-Asn-Xaa<sub>5</sub>-Asp-Cys-Arg (SEQ ID NO:169),

wherein Xaa<sub>1</sub> is Glu or  $\gamma$ -carboxy-Glu (Gla); Xaa<sub>2</sub> is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa<sub>3</sub> is Trp (D or L), halo-Trp or neo-Trp; Xaa<sub>4</sub> is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa<sub>5</sub> is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group, or derivatives thereof.

12. The substantially pure  $\alpha$ -conotoxin peptide of claim 11, wherein Xaa<sub>2</sub> is Lys.
13. The substantially pure  $\alpha$ -conotoxin peptide of claim 11, wherein Xaa<sub>1</sub> is Glu.
14. The substantially pure  $\alpha$ -conotoxin peptide of claim 11, wherein Xaa<sub>3</sub> is Trp.
15. The substantially pure  $\alpha$ -conotoxin peptide of claim 11, wherein Xaa<sub>4</sub> is Tyr.
- 25 16. The substantially pure  $\alpha$ -conotoxin peptide of claim 11, wherein Xaa<sub>4</sub> is mono-iodo-Tyr.
17. The substantially pure  $\alpha$ -conotoxin peptide of claim 11, wherein Xaa<sub>4</sub> is di-iodo-Tyr.

18. The substantially pure  $\alpha$ -conotoxin peptide of claim 10, which is modified to contain an O-glycan, an S-glycan or an N-glycan.
19. The substantially pure  $\alpha$ -conotoxin peptide of claim 11 which is modified to contain an O-glycan, an S-glycan or an N-glycan.
- 5 20. A substantially pure  $\alpha$ -conotoxin peptide having the generic formula III: Xaa<sub>1</sub>-Xaa<sub>2</sub>-Xaa<sub>3</sub>-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Cys-Cys-Xaa<sub>6</sub>-Xaa<sub>7</sub>-Xaa<sub>8</sub>-Xaa<sub>9</sub>-Cys-Xaa<sub>10</sub>-Xaa<sub>11</sub>-Xaa<sub>12</sub>-Xaa<sub>13</sub>-Xaa<sub>14</sub>-Xaa<sub>15</sub>-Xaa<sub>16</sub>-Cys-Xaa<sub>17</sub>-Xaa<sub>18</sub>-Xaa<sub>19</sub>-Xaa<sub>20</sub>-Xaa<sub>21</sub>-Xaa<sub>22</sub>-Xaa<sub>23</sub>-Xaa<sub>24</sub> (SEQ ID NO:3), wherein Xaa<sub>1</sub> is des-Xaa<sub>1</sub>, Ser or Thr; Xaa<sub>2</sub> is des-Xaa<sub>2</sub>, Asp, Glu,  $\gamma$ -carboxy-Glu (Gla), Asn, Ser or Thr; Xaa<sub>3</sub> is des-Xaa<sub>3</sub>, Ala, Gly, Asn, Ser, Thr, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>4</sub> is des-Xaa<sub>4</sub>, Ala, Val, Leu, Ile, Gly, Glu, Gla, Gln, Asp, Asn, Phe, Pro, hydroxy-Pro or any unnatural aromatic amino acid; Xaa<sub>5</sub> is des-Xaa<sub>5</sub>, Thr, Ser, Asp, Glu, Gla, Gln, Gly, Val, Asp, Asn, Ala, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>6</sub> is Thr, Ser, Asp, Asn, Met, Val, Ala, Gly, Leu, Ile, Phe, any unnatural aromatic amino acid, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>7</sub> is Ile, Leu, Val, Ser, Thr, Gln, Asn, Asp, Arg, His, halo-His, Phe, any unnatural aromatic amino acid, homoarginine, ornithine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>8</sub> is Pro, hydroxy-Pro, Ser, Thr, Ile, Asp, Leu, Val, Gly, Ala, Phe, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>9</sub> is Val, Ala, Gly, Ile, Leu, Asp, Ser, Thr, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>10</sub> is His, halo-His, Arg, homoarginine, ornithine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Asn, Ala, Ser, Thr, Phe, Ile, Leu, Gly, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>11</sub> is Leu, Gln, Val, Ile,

Gly, Met, Ala, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, Ser, Thr, Arg,  
homoarginine, ornithine, any unnatural basic amino acid, Asn, Glu, Gla, Gln, Phe, Trp (D  
or L), neo-Trp, halo-Trp or any unnatural aromatic amino acid; Xaa<sub>12</sub> is Glu, Gla, Gln, Asn,  
Asp, Pro, hydroxy-Pro, Ser, Gly, Thr, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-  
5 trimethyl-Lys, Arg, homoarginine, ornithine, any unnatural basic amino acid, Phe, His, halo-  
His, any unnatural aromatic amino acid, Leu, Met, Gly, Ala, Tyr, nor-Tyr, mono-halo-Tyr,  
di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing  
amino acid; Xaa<sub>13</sub> is His, halo-His, Asn, Thr, Ser, Ile, Val, Leu, Phe, any unnatural aromatic  
amino acid, Arg, homoarginine, ornithine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-  
10 trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr,  
O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid;  
Xaa<sub>14</sub> is Ser, Thr, Ala, Gln, Pro, hydroxy-Pro, Gly, Ile, Leu, Arg, ornithine, homoarginine,  
Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino  
acid; Xaa<sub>15</sub> is Asn, Glu, Gla, Asp, Gly, His, halo-His, Ala, Leu, Gln, Arg, ornithine,  
homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural  
basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr,  
nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa<sub>16</sub> is Met, Ile, Thr, Ser, Val,  
Leu, Pro, hydroxy-Pro, Phe, any unnatural aromatic amino acid, Tyr, nor-Tyr, mono-halo-  
Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, any unnatural hydroxy  
containing amino acid, Glu, Gla, Ala, His, halo-His, Arg, ornithine, homoarginine, Lys, N-  
15 methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid;  
Xaa<sub>17</sub> is des-Xaa<sub>17</sub>, Gly, Asp, Asn, Ala, Ile, Leu, Ser, Thr, His, halo-His, Arg, ornithine,  
homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any  
unnatural basic amino acid; Xaa<sub>18</sub> is des-Xaa<sub>18</sub>, Gly, Glu, Gla, Gln, Trp (D or L), neo, halo-  
Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys,  
20 N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>19</sub> is des-  
Xaa<sub>19</sub>, Ser, Thr, Val, Ile, Ala, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-  
dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>20</sub> is des-Xaa<sub>20</sub>,  
Val, Asp, His, halo-His, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-  
Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>21</sub> is des-Xaa<sub>21</sub>, Asn, Pro  
25 or hydroxy-Pro; Xaa<sub>22</sub> is des-Xaa<sub>22</sub>, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-  
dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa<sub>23</sub> is des-Xaa<sub>23</sub>,

Ser or Thr; Xaa<sub>24</sub> is des-Xaa<sub>24</sub>, Leu, Ile or Val; and the C-terminus contains a free carboxyl group or an amide group, with the proviso that (a) Xaa<sub>5</sub> is not Gly, when Xaa<sub>1</sub> is des-Xaa<sub>1</sub>, Xaa<sub>2</sub> is des-Xaa<sub>2</sub>, Xaa<sub>3</sub> is des-Xaa<sub>3</sub>, Xaa<sub>4</sub> is des-Xaa<sub>4</sub>, Xaa<sub>6</sub> is Ser, Xaa<sub>7</sub> is His, Xaa<sub>8</sub> is Pro, Xaa<sub>9</sub> is Ala, Xaa<sub>10</sub> is Ser, Xaa<sub>11</sub> is Val, Xaa<sub>12</sub> is Asn, Xaa<sub>13</sub> is Asn, Xaa<sub>14</sub> is Pro, Xaa<sub>15</sub> is Asp, Xaa<sub>16</sub> is Ile, Xaa<sub>17</sub> is des-Xaa<sub>17</sub>, Xaa<sub>18</sub> is des-Xaa<sub>18</sub>, Xaa<sub>19</sub> is des-Xaa<sub>19</sub>, Xaa<sub>20</sub> is des-Xaa<sub>20</sub>, Xaa<sub>21</sub> is des-Xaa<sub>21</sub>, Xaa<sub>22</sub> is des-Xaa<sub>22</sub>, Xaa<sub>23</sub> is des-Xaa<sub>23</sub>, and Xaa<sub>24</sub> is des-Xaa<sub>24</sub>.

21. A substantially pure  $\alpha$ -conotoxin peptide of generic formula III selected from the group consisting of:

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Val-Cys-His-Leu-Xaa<sub>1</sub>-His-Ser-Asn-Met-Cys (SEQ ID NO:22);

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Val-Cys-Arg-Gln-Asn-Asn-Ala-Xaa<sub>1</sub>-Xaa<sub>4</sub>-Cys-Arg (SEQ ID NO:23);

Xaa<sub>5</sub>-Gln-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Arg (SEQ ID NO:24);

Xaa<sub>5</sub>-Xaa<sub>1</sub>-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Arg (SEQ ID NO:25);

Xaa<sub>5</sub>-Gln-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Asp (SEQ ID NO:26);

Xaa<sub>5</sub>-Arg-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Arg (SEQ ID NO:27);

Xaa<sub>5</sub>-Gln-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Gly-Ile-Cys-Arg (SEQ ID NO:28);

Xaa<sub>5</sub>-Gln-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Thr-Cys-Arg (SEQ ID NO:29);

Xaa<sub>5</sub>-Gln-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Val-Cys-Arg (SEQ ID NO:30);

Xaa<sub>5</sub>-Gln-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Ile-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Arg (SEQ ID NO:31);

Xaa<sub>5</sub>-Gln-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Arg-Arg-Arg (SEQ ID NO:32);

Gly-Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ala-Val-Asn-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys  
(SEQ ID NO:33);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ser-Val-Asn-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys (SEQ ID  
NO:34);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys (SEQ ID  
NO:35);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ser-Gly-Xaa<sub>2</sub>-Thr-Gln-Xaa<sub>1</sub>-Xaa<sub>5</sub>-Cys-Arg-  
Xaa<sub>1</sub>-Ser (SEQ ID NO:36);

Xaa<sub>5</sub>-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ser-Gly-Asn-Asn-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Phe-Cys-Arg-Gln  
(SEQ ID NO:37);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ser-Gly-Asn-Asn-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Phe-Cys-Arg-Gln  
(SEQ ID NO:38);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ala-Met-Asn-Asn-Xaa<sub>5</sub>-Asp-Xaa<sub>4</sub>-Cys (SEQ  
ID NO:39);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Phe-Leu-Asn-Asn-Xaa<sub>5</sub>-Asp-Xaa<sub>4</sub>-Cys (SEQ  
ID NO:40);

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ile-Ala-Xaa<sub>2</sub>-Asn-Xaa<sub>5</sub>-His-Met-Cys-Gly  
(SEQ ID NO:41);

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Ala-Cys-Ala-Gly-Asn-Asn-Xaa<sub>5</sub>-His-Val-Cys-Arg-Gln  
(SEQ ID NO:43);

Gly-Cys-Cys-Ser-Arg-Xaa<sub>5</sub>-Ala-Cys-Ile-Ala-Asn-Asn-Xaa<sub>5</sub>-Asp-Leu-Cys (SEQ ID  
NO:44);

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Val-Cys-His-Val-Xaa<sub>1</sub>-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys-Arg-  
Arg-Arg-Arg (SEQ ID NO:45);

Gly-Gly-Cys-Cys-Ser-Phe-Xaa<sub>5</sub>-Ala-Cys-Arg-Xaa<sub>2</sub>-Xaa<sub>5</sub>-Arg-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Met-Cys-  
Gly (SEQ ID NO:46);

Xaa<sub>5</sub>-Xaa<sub>1</sub>-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Asn-Ser-Ser-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys-  
Gly (SEQ ID NO:47);

Xaa<sub>5</sub>-Gln-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Asn-Val-Gly-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys-  
Gly (SEQ ID NO:48);

Xaa<sub>5</sub>-Val-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Asn-Val-Gly-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Gly  
(SEQ ID NO:49);

Gly-Cys-Cys-Ser-Arg-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ile-Ala-Asn-Asn-Xaa<sub>5</sub>-Asp-Leu-Cys (SEQ ID NO:50);

Xaa<sub>5</sub>-Gln-Cys-Cys-Ser-His-Leu-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Arg (SEQ ID NO:51);

5 Gly-Cys-Cys-Ser-Xaa<sub>4</sub>-Phe-Asp-Cys-Arg-Met-Met-Phe-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Met-Cys-Gly-Xaa<sub>3</sub>-Arg (SEQ ID NO:52);

Gly-Gly-Cys-Cys-Ser-Phe-Ala-Ala-Cys-Arg-Xaa<sub>2</sub>-Xaa<sub>4</sub>-Arg-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Met-Cys-Gly (SEQ ID NO:53);

10 Gly-Gly-Cys-Cys-Phe-His-Xaa<sub>5</sub>-Val-Cys-Xaa<sub>4</sub>-Ile-Asn-Leu-Leu-Xaa<sub>1</sub>-Met-Cys-Arg Gln-Arg (SEQ ID NO:54);

Ser-Ala-Thr-Cys-Cys-Asn-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Xaa<sub>4</sub>-Xaa<sub>1</sub>-Thr-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ser-Cys-Leu (SEQ ID NO:55);

15 Ala-Cys-Cys-Ala-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Phe-Xaa<sub>1</sub>-Ala-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Arg-Cys-Leu (SEQ ID NO:56);

Asn-Ala-Xaa<sub>1</sub>-Cys-Cys-Xaa<sub>4</sub>-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Xaa<sub>4</sub>-Xaa<sub>1</sub>-Ala-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Leu (SEQ ID NO:57);

20 Xaa<sub>1</sub>-Cys-Cys-Thr-Asn-Xaa<sub>5</sub>-Val-Cys-His-Ala-Xaa<sub>1</sub>-His-Gln-Xaa<sub>1</sub>-Leu-Cys-Ala-Arg-Arg-Arg (SEQ ID NO:170);

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Val-Cys-His-Leu-Xaa<sub>1</sub>-His-Ser-Asn-Leu-Cys (SEQ ID NO:171);

25 Xaa<sub>1</sub>-Cys-Cys-Thr-Asn-Xaa<sub>5</sub>-Val-Cys-His-Val-Xaa<sub>1</sub>-His-Gln-Xaa<sub>1</sub>-Leu-Cys-Ala-Arg-Arg-Arg (SEQ ID NO:172);

Xaa<sub>6</sub>-Xaa<sub>1</sub>-Cys-Cys-Ser-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Ala-Cys-Asn-Leu-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys (SEQ ID NO:173);

30 Xaa<sub>5</sub>-Xaa<sub>1</sub>-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Asn-Ser-Thr-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys-Gly (SEQ ID NO:174);

Leu-Asn-Cys-Cys-Met-Ile-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Xaa<sub>3</sub>-Xaa<sub>2</sub>-Xaa<sub>2</sub>-Xaa<sub>4</sub>-Gly-Asp-Arg-Cys-Ser-Xaa<sub>1</sub>-Val-Arg (SEQ ID NO:175);

Ala-Phe-Gly-Cys-Cys-Asp-Leu-Ile-Xaa<sub>5</sub>-Cys-Leu-Xaa<sub>1</sub>-Arg-Xaa<sub>4</sub>-Gly-Asn-Arg-Cys-Asn-Xaa<sub>1</sub>-Val-His (SEQ ID NO:176);

Leu-Gly-Cys-Cys-Asn-Val-Thr-Xaa<sub>5</sub>-Cys-Xaa<sub>3</sub>-Xaa<sub>1</sub>-Xaa<sub>2</sub>-Xaa<sub>4</sub>-Gly-Asp-Xaa<sub>2</sub>-Cys-Asn-Xaa<sub>1</sub>-Val-Arg (SEQ ID NO:177);

Asp-Xaa<sub>1</sub>-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Ala-Cys-Arg-Val-Asn-Asn-Xaa<sub>5</sub>-His-Val-Cys-Arg-Arg-Arg (SEQ ID NO:178);

Leu-Asn-Cys-Cys-Ser-Ile-Xaa<sub>5</sub>-Gly-Cys-Xaa<sub>3</sub>-Asn-Xaa<sub>1</sub>-Xaa<sub>4</sub>-Xaa<sub>2</sub>-Asp-Arg-Cys-Ser-Xaa<sub>2</sub>-Val-Arg (SEQ ID NO:179);

Gly-Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Val-Cys-Xaa<sub>4</sub>-Phe-Asn-Asn-Xaa<sub>5</sub>-Gln-Met-Cys-Arg (SEQ ID NO:180);

Gly-Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Val-Cys-Asn-Leu-Asn-Asn-Xaa<sub>5</sub>-Gln-Met-Cys-Arg (SEQ ID NO:181);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Xaa<sub>4</sub>-Ala-Asn-Asn-Gln-Ala-Xaa<sub>4</sub>-Cys-Asn (SEQ ID NO:182);

Gly-Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ser-Val-Thr-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys (SEQ ID NO:183);

Gly-Gly-Cys-Cys-Ser-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Ala-Cys-Ser-Val-Xaa<sub>1</sub>-His-Gln-Asp-Leu-Cys-Asp (SEQ ID NO:184);

Val-Ser-Cys-Cys-Val-Val-Arg-Xaa<sub>5</sub>-Cys-Xaa<sub>3</sub>-Ile-Arg-Xaa<sub>4</sub>-Gln-Xaa<sub>1</sub>-Xaa<sub>1</sub>-Cys-Leu-Xaa<sub>1</sub>-Ala-Asp-Xaa<sub>5</sub>-Arg-Thr-Leu (SEQ ID NO:185);

Xaa<sub>6</sub>-Asn-Cys-Cys-Ser-Ile-Xaa<sub>5</sub>-Gly-Cys-Xaa<sub>3</sub>-Xaa<sub>1</sub>-Xaa<sub>2</sub>-Xaa<sub>4</sub>-Gly-Asp-Xaa<sub>2</sub>-Cys-Ser-Xaa<sub>1</sub>-Val-Arg (SEQ ID NO:186);

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Val-Cys-His-Leu-Xaa<sub>1</sub>-His-Xaa<sub>5</sub>-Asn-Ala-Cys (SEQ ID NO:187);

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Ile-Cys-Xaa<sub>4</sub>-Phe-Asn-Asn-Xaa<sub>5</sub>-Arg-Ile-Cys-Arg (SEQ ID NO:188);

Xaa<sub>1</sub>-Cys-Cys-Ser-Gln-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Arg-Xaa<sub>3</sub>-Xaa<sub>2</sub>-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys-Ser (SEQ ID NO:189);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ala-Gly-Asn-Asn-Gln-His-Ile-Cys (SEQ ID NO:190);

Gly-Cys-Cys-Ala-Val-Xaa<sub>5</sub>-Ser-Cys-Arg-Leu-Arg-Asn-Xaa<sub>5</sub>-Asp-Leu-Cys-Gly-Gly (SEQ ID NO:191);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asn-Asn-Xaa<sub>5</sub>-His-Ile-Cys (SEQ ID NO:192);

Thr-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Xaa<sub>1</sub>-Cys-Cys-Xaa<sub>5</sub>-Asn-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Phe-Ala-Thr-Asn-Ser-Asp-Ile-Cys-Gly (SEQ ID NO:193);

Asp-Ala-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Ser-Gly-Xaa<sub>2</sub>-His-Gln-Asp-Leu-Cys(SEQ ID NO:194);

Xaa<sub>1</sub>-Asp-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Ser-Val-Gly-His-Gln-Asp-Leu-Cys(SEQ ID NO:195);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ala-Gly-Ser-Asn-Ala-His-Ile-Cys (SEQ ID NO:196);

Xaa<sub>1</sub>-Asp-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Ser-Val-Gly-His-Gln-Asp-Met-Cys (SEQ ID NO:197);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ala-Gly-Asn-Asn-Xaa<sub>5</sub>-His-Ile-Cys (SEQ ID NO:198);

Gly-Cys-Cys-Gly-Asn-Xaa<sub>5</sub>-Ser-Cys-Ser-Ile-His-Ile-Xaa<sub>5</sub>-Xaa<sub>4</sub>-Val-Cys-Asn (SEQ ID NO:199);

Thr-Asp-Ser-Xaa<sub>1</sub>-Xaa<sub>1</sub>-Cys-Cys-Leu-Asp-Ser-Arg-Cys-Ala-Gly-Gln-His-Gln-Asp-Leu-Cys-Gly (SEQ ID NO:200);

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Xaa<sub>4</sub>-Ala-Asn-Asn-Gln-Ala-Xaa<sub>4</sub>-Cys-Asn (SEQ ID NO:201);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ser-Val-Asn-Asn-Xaa<sub>5</sub>-Asp-Ile-Cys (SEQ ID NO:202);

Gly-Xaa<sub>2</sub>-Cys-Cys-Ile-Asn-Asp-Ala-Cys-Arg-Ser-Xaa<sub>2</sub>-His-Xaa<sub>5</sub>-Gln-Xaa<sub>4</sub>-Cys-Ser (SEQ ID NO:203);

Gly-Cys-Cys-Xaa<sub>4</sub>-Asn-Ile-Ala-Cys-Arg-Ile-Asn-Asn-Xaa<sub>5</sub>-Arg-Xaa<sub>4</sub>-Cys-Arg(SEQ ID NO:204);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Val-Cys-Arg-Phe-Asn-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>2</sub>-Xaa<sub>4</sub>-Cys-Gly (SEQ ID NO:205);

Asp-Xaa<sub>1</sub>-Cys-Cys-Ala-Ser-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Arg-Leu-Asn-Asn-Xaa<sub>5</sub>-Xaa<sub>4</sub>-Val-Cys-His (SEQ ID NO:206);

Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Val-Cys-Xaa<sub>3</sub>-Gln-Asn-Asn-Ala-Xaa<sub>1</sub>-Xaa<sub>4</sub>-Cys-Arg-Xaa<sub>1</sub>-Ser (SEQ ID NO:207);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ala-Gln-Asn-Asn-Gln-Asp-Xaa<sub>4</sub>-Cys (SEQ ID NO:208);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ser-Gly-Asn-Asn-Arg-Xaa<sub>1</sub>-Xaa<sub>4</sub>-Cys-Arg-Xaa<sub>1</sub>-Ser (SEQ ID NO:209);

Asp-Xaa<sub>5</sub>-Cys-Cys-Ser-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Asp-Cys-Gly-Ala-Asn-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Gly (SEQ ID NO:210);

Xaa<sub>1</sub>-Cys-Cys-Ser-Gln-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Arg-Xaa<sub>3</sub>-Xaa<sub>2</sub>-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys-Ser (SEQ ID NO:211);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Ala-Gly-Asn-Asn-Xaa<sub>5</sub>-His-Ile-Cys (SEQ ID NO:212);

Gly-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Ser-Cys-Asn-Val-Asn-Asn-Xaa<sub>5</sub>-Asp-Xaa<sub>4</sub>-Cys (SEQ ID NO:213);

Xaa<sub>1</sub>-Xaa<sub>1</sub>-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys-Ser-Val-Gly-His-Gln-Asp-Met-Cys-Arg (SEQ ID NO:214);

Gly-Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Ala-Cys-Leu-Val-Asn-His-Leu-Xaa<sub>1</sub>-Met-Cys (SEQ ID NO:215);

Arg-Asp-Xaa<sub>5</sub>-Cys-Cys-Phe-Asn-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asn-Asn-Xaa<sub>5</sub>-Gln-Ile-Cys (SEQ ID NO:216);

Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Ser-Cys-Xaa<sub>3</sub>-Arg-Leu-His-Ser-Leu-Ala-Cys-Thr-Gly-Ile-Val-Asn-Arg (SEQ ID NO:217);

Cys-Cys-Thr-Asn-Xaa<sub>5</sub>-Ala-Cys-Leu-Val-Asn-Asn-Ile-Arg-Phe-Cys-Gly (SEQ ID NO:218);

Asp-Xaa<sub>1</sub>-Cys-Cys-Ser-Asp-Xaa<sub>5</sub>-Arg-Cys His-Gly-Asn-Asn-Arg-Asp-His-Cys-Ala (SEQ ID NO:219);

Asp-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Leu-Cys-Arg-Leu-Phe-Val Xaa<sub>5</sub>-Gly-Leu-Cys-Ile (SEQ ID NO:220);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Val-Cys-Xaa<sub>2</sub>-Val-Arg-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Asp-Leu-Cys-Arg (SEQ ID NO:221);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asn-Asn-Xaa<sub>5</sub>-His-Ile-Cys (SEQ ID NO:222);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Val-Cys-Xaa<sub>2</sub>-Val-Arg-Xaa<sub>4</sub>-Ser-Asp-Met-Cys (SEQ ID NO:223);

Gly-Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Xaa<sub>2</sub>-Val-His-Phe-Xaa<sub>5</sub>-His-Ser-Cys (SEQ ID NO:224);

Val-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Val-Cys-His-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Leu-Cys-Arg-Arg-Arg (SEQ ID NO:225);

Gly-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Val-Cys-Asn-Leu-Ser-Asn-Xaa<sub>5</sub>-Gln-Ile-Cys-Arg (SEQ ID NO:226);

Xaa<sub>6</sub>-Xaa<sub>1</sub>-Cys-Cys-Ser-His-Xaa<sub>5</sub>-Ala-Cys-Asn-Val-Asp-His-Xaa<sub>5</sub>-Xaa<sub>1</sub>-Ile-Cys-Arg (SEQ ID NO:227);

5 Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Ala-Cys-Leu-Val-Asn-His-Ile-Arg-Phe-Cys-Gly (SEQ ID NO:228);

Asp-Cys-Cys-Asp-Asp-Xaa<sub>5</sub>-Ala-Cys-Thr-Val-Asn-Asn-Xaa<sub>5</sub>-Gly-Leu-Cys-Thr (SEQ ID NO:229); and

10 Gly-Cys-Cys-Ser-Asn-Xaa<sub>5</sub>-Xaa<sub>5</sub>-Cys-Ile-Ala/Xaa<sub>2</sub>-Asn-Xaa<sub>5</sub>-His-Met-Cys-Gly-Gly-Arg-Arg (SEQ ID NO:230),

wherein Xaa<sub>1</sub> is Glu or  $\gamma$ -carboxy-Glu (Gla); Xaa<sub>2</sub> is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa<sub>3</sub> is Trp (D or L), halo-Trp or neo-Trp; Xaa<sub>4</sub> is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa<sub>5</sub> is Pro or hydroxy-Pro; Xaa<sub>6</sub> is Gln or pyro-Glu; and the C-terminus contains a carboxyl or amide group, or derivatives thereof.

- 15
22. The substantially pure  $\alpha$ -conotoxin peptide of claim 21, wherein Xaa<sub>2</sub> is Lys.
23. The substantially pure  $\alpha$ -conotoxin peptide of claim 21, wherein Xaa<sub>1</sub> is Glu.
24. The substantially pure  $\alpha$ -conotoxin peptide of claim 21, wherein Xaa<sub>3</sub> is Trp.
25. The substantially pure  $\alpha$ -conotoxin peptide of claim 21, wherein Xaa<sub>4</sub> is Tyr.
- 20 26. The substantially pure  $\alpha$ -conotoxin peptide of claim 21, wherein Xaa<sub>4</sub> is mono-iodo-Tyr.
27. The substantially pure  $\alpha$ -conotoxin peptide of claim 21, wherein Xaa<sub>4</sub> is di-iodo-Tyr.
28. The substantially pure  $\alpha$ -conotoxin peptide of claim 20, which is modified to contain an O-glycan, an S-glycan or an N-glycan.

29 The substantially pure  $\alpha$ -conotoxin peptide of claim 21 which is modified to contain an O-glycan, an S-glycan or an N-glycan.

30. A substantially pure  $\alpha$ -conotoxin peptide selected from the group consisting of:

Cys-Cys-Thr-Ile-Xaa<sub>5</sub>-Ser-Cys-Xaa<sub>4</sub>-Xaa<sub>1</sub>-Xaa<sub>2</sub>-Xaa<sub>2</sub>-Ile-Xaa<sub>2</sub>-Ala-Cys-Val-Phe (SEQ ID NO:231) and

Gly-Cys-Cys-Gly-Asn-Xaa<sub>5</sub>-Ala-Cys-Ser-Gly-Ser-Ser-Xaa<sub>2</sub>-Asp-Ala-Xaa<sub>5</sub>-Ser-Cys (SEQ ID NO:232),

wherein Xaa<sub>1</sub> is Glu or  $\gamma$ -carboxy-Glu (Gla); Xaa<sub>2</sub> is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa<sub>4</sub> is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa<sub>5</sub> is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group, or derivatives thereof.

31. The substantially pure  $\alpha$ -conotoxin peptide of claim 30, wherein Xaa<sub>2</sub> is Lys.

32. The substantially pure  $\alpha$ -conotoxin peptide of claim 30, wherein Xaa<sub>1</sub> is Glu.

33. The substantially pure  $\alpha$ -conotoxin peptide of claim 30, wherein Xaa<sub>4</sub> is Tyr.

15 34. The substantially pure  $\alpha$ -conotoxin peptide of claim 30, wherein Xaa<sub>4</sub> is mono-iodo-Tyr.

35. The substantially pure  $\alpha$ -conotoxin peptide of claim 30, wherein Xaa<sub>4</sub> is di-iodo-Tyr.

36. The substantially pure  $\alpha$ -conotoxin peptide of claim 30, which is modified to contain an O-glycan, an S-glycan or an N-glycan.

20 37. An isolated nucleic acid comprising a nucleic acid coding for an  $\alpha$ -conotoxin precursor comprising an amino acid sequence selected from the group of amino acid sequences set forth in Tables 1-134.

38. The nucleic acid of claim 37 wherein the nucleic acid comprises a nucleotide sequence selected from the group of nucleotide sequences set forth in Tables 1-134 or their complements.
39. A substantially pure  $\alpha$ -conotoxin protein precursor comprising an amino acid sequence selected from the group of amino acid sequences set forth in Tables 1-134.